Australian Government
Department of Health and Ageing
Therapeutic Goods Administration

Prescription medicine
BPR update newsletter

April 2011

The TGA—*Safeguarding public health through the effective and timely regulation of therapeutic goods*

Introduction

The April edition of the *Prescription medicine BPR update newsletter* provides an update of the three projects under the Business Process Reform Program.

In this edition:

- Streamlined submission process (SSP)
- Product information/consumer medicine information (PI/CMI)
- Australian Public Assessment Records (AusPAR)
- Industry Working Group report
- Consultation on electronic submission dossier requirements.

The *Prescription medicine BPR update newsletter* (BPR update) reports on progress in the BPR program. Each month, the *BPR update* reports on the progress of the streamlined submission process. Each quarter, an update is provided on the PI/CMI project and the AusPAR project.

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http://www.tga.gov.au/about/tga-bpi-pm-bpr.htm

1—Streamlined submission process project

1.1 Progress to date

	Batch					
Item	**November**	**December**	**January**	**February**	**March**	**April**
Pre-submission planning forms						
Date processing PPFs commenced	1 Nov 10	1 Dec 10	1 Jan 11	1 Feb 11	1 Mar 11	1 Apr 11
PPFs received by processing date	28	34	24	25	27	33
S. 31 response—sponsor nominated 60 day	46%	68%	38%	48%	52%	61%
Assessment status						
Number incomplete	5	3	2	1	pending	pending
Number withdrawn or deferred	n/a	1	1	3	pending	pending
Deficiencies (48 hours to address)	n/a	4	3	6	pending	pending
Progress to planning letter	23	30	21	21	pending	pending
Application type						
New entity – A	2	4	3	2	2	2
New fixed dose combination – B	0	1	1	1	0	0
Extension of indication – C	10	2	3	0	2	1
Generic – D	8	12	8	11	9	20
Minor variation – J, G, H	4	11	5	7	12	6
Major variation – F	3	2	1	4	2	4
(multiple application types)	2 with 3	2 with 2	3 with 2	-	-	-
M1 – Outcome of pre-submission sent						
M1 target date	15 Dec 10	15 Jan 11	15 Feb 11	15 Mar 11	15 Apr 11	15 May 11
Number met target date	23	30	21	4	pending	pending
M2 – Outcome of submission consideration sent						
M2 target date	31 Jan 10	28 Feb 11	31 Mar 11	30 Apr 11	31 May 11	30 June 11
Number withdrawn	-	3[#]	3[§]	pending	pending	pending
Deficiencies (48 hours to address)	15	12	9[@]	pending	pending	pending
Number met target date	21	11	11	pending	pending	pending
Number effective notification letter	20	27	19*[@]	pending	pending	pending
Number not effective notification letter	3	0	1	pending	pending	pending

[#] Includes 1 submission that was deferred until March 2011.

[§] Includes 2 submissions that were re-lodged for consideration in the February batch.

* Includes 1 submission that was deferred from the December batch.

[@] At the time of writing, the TGA is yet to decide on the effectiveness of 2 submissions with deficiencies.

1.2 Pre-submission planning form—regulatory requirements

The following information draws on common issues identified with PPFs submitted to date under the streamlined submission process. This information will assist sponsors in meeting the regulatory requirements of the streamlined submission process.

Problem	TGA requirement
Draft comprehensive table of contents	Sponsors must attached a draft comprehensive table of contents to the pre-submission planning form (PPF). It must: · include the full names of study titles · include full details of literature references (including the title, author, and page number) to be provided in modules 4.3 and 5.4 of the submission dossier. The full details of each reference are required for the TGA to determine whether or not evaluation is required, and if so, to assess the resources required to undertake the evaluation. *See—* Section 2.2 of *Information for sponsors completing the pre-submission planning form*.

1.3 Guidance for an effective submission

The following information identifies some regulatory requirements which are not being met, thereby risking that a submission will be considered not effective.

Problem	TGA requirement
Module 1 compliance	In September 2010, the TGA released a revised CTD Module 1 that: · aimed to provide more clarity to sponsors on the requirements for preparing module 1 of the submission dossier · introduced additional requirements for preparing module 1 under the streamlined submission process. The January 2011 version included minor corrections and further clarifications. The TGA has processed three batches of submission dossiers under the streamlined submission process and has noted a large proportion of submissions do not comply with the revised CTD Module 1 requirements. Sponsors should ensure they are familiar with the revised CTD Module 1—January 2011 and their submission dossiers comply with this version. *See—* *CTD Module 1—Administrative information and prescribing information for Australia* January 2011.

Problem	TGA requirement
Module 1.8.3	A common deficiency in submission dossiers is the failure to provide Module 1.8.3 or to provide a Module 1.8.3 that is compliant with requirements as established in CTD Module 1. Module 1.8.3 must: · be included for all submissions for which a PPF has been lodged · contain a declaration that either: o states that the submission is consistent with the PPF lodged, or o lists any inconsistencies with an appropriate explanation · identify how the sponsor has addressed any issues requiring sponsor action raised by the TGA in the planning letter. *See—* Module 1.8.3 of *CTD Module 1—Administrative information and prescribing information for Australia* January 2011.
Choice of media—CD or DVD	For the electronic copy of the submission dossier: · re-writable disks are not acceptable · sponsors must use the smallest number of media units possible. If a submission will not fit on a single CD, it should be provided on a DVD, rather than being split across several CDs. *See—* Requirements for electronic submission dossier in *CTD Module 1—Administrative information and prescribing information for Australia* January 2011.
Electronic copy submission dossiers	The TGA has received a number of electronic copies of submission dossiers which are missing data. In the letter of application, sponsors declare the electronic copy of the submission dossier is identical to the paper copy and should ensure this is the case before lodging their submission dossier. *See—* Module 1.0.1—Letter of application in *CTD Module 1—Administrative information and prescribing information for Australia* January 2011.

1.4 Contact

Email: streamlinedsubmission@tga.gov.au

2—PI/CMI project

The PI/CMI project seeks to improve access for consumers and health professionals to information about prescription medicines by providing a single trusted internet source for product information (PI) and consumer medicine information (CMI) documents.

To achieve this, the TGA collects the following:

- PI documents for all prescription medicines registered on the Australian Register of Therapeutic Goods (ARTG), whether they are marketed or not[1]
- CMI documents for all registered prescription medicines on the ARTG that are being marketed in Australia.

In addition to supplying PI and CMI documents for existing registrations, it is a requirement that sponsors lodge PIs and CMIs with the TGA following approval of applications for new and varied products. The requirements for PI and CMI lodgement are identified in the approval letter and can also be found on the Improved access to information page on the TGA website. Lodgement of PI and CMI documents must be completed electronically via the secure eBS facility or healthlinks.net.

Published PI and CMI documents are available on the TGA eBS website at http://ww.ebs.tga.gov.au under 'Public TGA information'.

2.1 PI/CMI progress

The following table shows progress in collecting PI and CMI documents as at 30 March 2011.

Document	As percentage of prescription medicine entries on ARTG	
	January 2011	March 2011
PI	71%	81%
CMI	54.3%	58.29%
Total ARTG entries		10,043

2.2 Key areas for sponsors

Lodging an updated PI

The TGA is receiving inquiries from sponsors who have lodged an updated PI using the replace function but cannot see the updated PI on the TGA eBS PI/CMI facility. This happens when the 'replace' draft has not been lodged correctly. When not lodged correctly, TGA eBS creates a draft which is automatically saved in the 'draft view'. To locate the previously lodged PI document, sponsors must open the draft from the drafts view by selecting 'view drafts' from the 'portal' drop-down menu. The sponsor must then either:

- check the draft information, attach the current PDF document, validate, and then lodge
- delete the PI, then complete the replace process by using the 'replace' option which will now be visible.

If sponsors are unable to locate their previously lodged PI under the drafts view, they should then contact the TGA for further advice.

[1] The TGA acknowledges there are a number of registered prescription medicines which, for a range of legitimate reasons, may not have a PI, for example, grandfathered products.

PI—for publication/not for publication
For all prescription medicines registered on the ARTG, product information (PI) must be uploaded and marked 'for publication' (for prescription medicines currently being marketed), or 'not for publication' (for prescription medicines currently not being marketed). This requirement for a PI does not apply to grandfathered products.

2.3 TGA activities

Outstanding PI and CMI documents
To date, the TGA has completed telephone contact with each of the 55 sponsors who have failed to lodge PI and CMI documents. Forty sponsors have yet to submit the documents, or to advise on reasons for being unable to submit the required documents. In accordance with the advice from the Industry Working Group, the TGA is reviewing mechanisms to ensure compliance from the sponsors with outstanding documents.

2.4 Contact

Email: prescriptions.pi@tga.gov.au.

3—AusPAR project

3.1 AusPAR progress to date

The following table provides an update on AusPAR progress to 31 March 2011.

Status	Number	
	January 2011	March 2011
Total drafted	108	126
Released on TGA website	74	102
With sponsors for comment	4	7
Waiting for either: · the appeal period for the delegate's decision on the application to end · the result of an appeal in relation to the delegate's decision prior to the document being released	2	4
Initial draft complete and waiting for the delegate's decision	16	6
Undergoing final internal TGA quality assurance review	12	7

3.2 AusPAR consultation

The TGA will undertake a consultation process shortly to canvass views on some of the issues concerning AusPARs, including format and scope of the AusPAR, sponsor compliance with the two week period for comment, commercially confidential material, and a shared understanding of the scope of response for sponsor review.

Further information will be provided on the TGA website and in the *BPR Update*.

3.3 Contact

Email: auspars@tga.gov.au.

4—Other news

4.1 IWG report

The following table summarises the draft actions and outcomes arising from the 7 March 2011 Industry Working Group (IWG) meeting.

	Action
1—Introduction and overview of previous actions	
1.2	IWG reviewed the actions from previous meeting: *Action Mar 11/1*— IWG Membership. TGA to clarify status of the involvement of Ausbiotech on IWG. Members noted the new members from Aspen, Hospira and Apotex. Members noted that under the terms of reference, IWG members are not representative of sponsors and substitute persons are not encouraged. *Action Mar 11/2*—IWG agreed that separate sub-working group role in developing a module 2 equivalent template will be progressed at the next meeting in the broader context of M1 and M2 review. IWG agreed that the current '6 month' clearance for GMP be reviewed later in the transition phase. *Action Mar 11/3*—TGA to present qualitative and quantitative performance measures to IWG at next meeting.
2—BPR program items for discussion/ noting	
2.3	**AusPAR consultation** IWG considered progress with AusPARs since commencement in Nov 2009 and the need for consultation to inform the further development of this initiative, and agreed the following: *Action Mar 11/4*—TGA to commence consultation (with consumers, health professionals, and industry) on AusPARs to seek advice on the following: · sponsor compliance with two week clearance timeframes and scope of response · confidential information—clarity of regulatory requirements · shared understanding of scope of response for sponsors · functionality of format, for example should list of studies in body with appendix for detail be made · scope for 2011 to include ACPM + generic medicines (approval letter + BE statement + PI) · option for consumer–specific one page summary · routine website statistics/routine online survey on usage of AusPAR information. *Action Mar 11/5*—TGA to conduct consultation in readiness for a report on outcomes to IWG at June meeting.
2.4	**PI/CMI project** IWG noted the outcomes from the 2nd round of back capture, however were concerned that 55 of the targeted 118 sponsors have yet to comply. *Action Mar 11/6*—IWG advised TGA to explore options for taking steps to cancel ARTG registration for products where sponsors do not submit PI/CMI information in response to TGA request letter. *Action Mar 11/7*—TGA to explore options to accurately account for legitimate absence of PI/CMI information—i.e. for products not marketed, grandfathered products, and remove from the target goal. *Action Mar 11/8*—Goal for June 2011to achieve 100% PI and 80% CMI, noting the removal of documents that cannot be provided.

2.5	**Fee arrangements** IWG noted and welcomed the progress of consultation with industry on the new fee arrangements to align with the new streamlined submission process.
3—Streamlined submission	

3.1	**Milestone 1**
	IWG discussed the performance and issues identified through the first 4 months of the streamlined submission process. Overall IWG agreed that the new process was on track and was meeting expectations, with minor areas for review and refinement. A key issue for consideration is the clarity of expectations and the delineation of assessment versus evaluation activities.
	
	Coordination team
	Action Mar 11/9—TGA to staff coordination team to full capacity to improve the delivery of coordinated and consistent communication with sponsors.
	
	Proposed changes to TGA processes (pending internal advice and noting that these arrangements are only intended to support sponsors during the transition phase)
	Action Mar 11/10—*Single administration deficiency assessment*—Upon receipt, the PPF will be assessed by TGA's administrative staff. Where deficiencies are identified, the TGA will contact sponsors by phone seeking clarification or provision of required documents to the required standard (e.g. signatures). Sponsors will be advised of the requirement to provide a single response, which is acceptable to the TGA, within a two working day timeframe or risk the PPF being considered not complete.
	Action Mar 11/11—*Single scientific/guidance deficiency assessment*—Upon completion of the administrative assessment, the PPF will be assessed by the TGA's scientific staff. Prior to issuing a planning letter (week 6), where deficiencies are identified, the TGA will contact sponsors by email (week 5) seeking clarification or provision of required documents to the mandatory standard.
	· The TGA will advise sponsors of all deficiencies, without judgement, allowing the sponsor to decide whether deficiencies can be rectified within the timeframe. This approach removes the need for the TGA to determine whether deficiencies are major or minor.
	· Sponsors will be advised of the requirement to provide a response, which is acceptable to the TGA, within a two working day timeframe.
	· If NO, or an inadequate response to deficiencies is received from the sponsor, within the required timeframe, the PPF will be considered NOT complete.
	· If the sponsor responds to the deficiencies to the required standard, a planning letter, confirming the PPF as complete, will be issued.
	Action Mar 11/12—*Justifications*—The declaration to be updated so that in lodging the PPF, the sponsor declares that:
	· their intended dossier fully complies with all relevant guidelines
	· all deviations from the guidelines will be detailed in a justification
	· the justification will fully satisfy any relevant standards for a robust scientific justification
	· the justification is highlighted in the PPF in accordance with the guidelines. (*see*—Section 2.3 of *Information for sponsors completing a pre-submission planning form*, January 2011)
	· In assessing the PPF the TGA will:
	  · note the sponsor's declaration (adherence to all guidelines and other requirements)
	  · note the existence of a justification(s) to explain all deviations from the required guidelines
	  · confirm the justification(s) meets the standard for a justification of its type

(where one exists), and if not, advise the sponsor of deficiencies in accordance with the standard processes for deficiency assessment

- upon response from the sponsor, the TGA will assess whether the justification meets the required standard (this does not constitute an evaluation of the justification but is an administrative assessment of whether the justification contains the required data)
    - if NO, the PPF is NOT complete
    - if YES, the PPF is complete. The planning letter may include advice to the sponsor about issues that may impair the submission during the submission or evaluation phase. This will allow the sponsor to make any amendment before submission.

Note—advice from the TGA in the planning letter provides information on issues a sponsor is encouraged to address before lodging the submission dossier. It does not indicate that the information (or justifications) will be considered favourably during the evaluation.

Action Mar 11/13—TGA to continually review and improve clarity of requirements through the development of the guidance documents.

Changes to the PPF/regulatory/guidance documents/templates

PPF form/help notes—*Action Mar 11/14*—TGA to make the following changes:

- highlight where sponsors are required to attach information and other documentation, e.g. justifications
- fields provided to record the details of two sponsor contacts (and ideally a generic email)
- improved clarification of requirements for justifications.

Mandatory requirements for pre-submission phase—*Action Mar 11/15*—To support transparency and consistency, TGA to develop mandatory requirements for considering PPF complete.

Q&A—*Action Mar 11/16*—*Fixed dose combinations*—TGA to update Q&A page to highlight need for sponsors to include with the PPF a letter of approval from the TGA for fixed dose combinations.

Action Mar 11/17—*Trade names*—TGA to update Q&A page to clarify process on trade names:

- advice to sponsors on self assessing their proposed trade names
- requirement that the number of trade names at PPF must equal the number of trade names at submission.

Planning letter—*Action Mar 11/18*—TGA to amend the template for planning letter to include:

- improved clarity on the deadline for the submission dossier to be received by the TGA (see milestone 2 for further actions on this matter)
- further information on reasons for a variation to a default milestone, where relevant (where the planning letter identifies variation to default milestones, the TGA will endeavour to discuss this with the sponsor prior to issuing the planning letter)
- standard placement for the following information:
    - issues the sponsor must address in their submission or risk the submission being considered not effective at the submission phase
    - issues that the TGA has noted that may place the positive evaluation of the submission at risk—sponsors can decide how or whether to act upon this information (for example, advice on justifications)
    - wording to emphasise that sponsor compliance with information/advice in the planning letter does not guarantee a submission will be considered effective and accepted for evaluation, nor does it imply the evaluation will result in a positive outcome.

3.2	**Milestone 2** ***Timeframes*** The IWG noted the significant constraints on the TGA in meeting the milestone 2 requirements within the 10 calendar day timeframe and discussed possible options to adjust the milestone dates between M1, submission delivery, and M2. Members noted the key issues are : · submissions being received at the last possible date impairing the TGA's ability to streamline entry processes · poor standard of physical dossiers · sponsor expectations of a right to respond at multiple levels prior to TGA consideration of a submission as effective/not effective currently generates a delay of up to six working days · the TGA's need to coordinate the consideration of a submission following assessment by a range of expertise and administrative functions · the need to ensure increased focus on assessing proposed submission quality at the M1 phase to prevent deficiencies at the M2 phase. The TGA noted the proposal from Medicines Australia that a central assessor function would improve timelines and consistency. However, the TGA advised this model excludes access to the correct expertise for assessing a submission, and would have the effect of disabling TGA's evaluation planning. The IWG agreed that the following actions are to be implemented with a view to monitoring impact on this milestone. *Action Mar 11/19*—The TGA to mandate lodgement of A, B, C submissions types one week earlier (8th of month). The TGA will remove reference to early delivery of large and complex submissions (but retain this size reference when in the context of M3 timelines). *Action Mar 11/20*—The TGA to implement increased focus on quality submissions at the M1 phase (see above recommendations regarding justifications). *Action Mar 11/21*—The TGA to remind sponsors of the mandatory requirements for physical and electronic submission dossier delivery. Failure to meet these requirements will result in a submission being considered not effective and not accepted for evaluation. ***Volume specification*** The IWG noted examples of inaccurate volume number statements and the significant impact this has on TGA planning and resourcing. The IWG advised that migration to page numbers was not feasible. *Action Mar 11/22*—TGA to continue the current arrangements for considering submissions to be not effective when there is a deviation from the planned versus actual submission and that sponsors are accountable for: · recording of planned volume numbers in PPF · recording of actual volume numbers in the submission cover letter, together with an explanation of any variation from the PPF. ***Electronic dossier requirements*** The IWG agreed on the importance of electronic dossiers to the success of the streamlined submission process and noted the status of the proposed NeeS regulatory and supporting documents. Members highlighted their concerns about industry readiness to comply. *Action Mar 11/23*—The TGA to advise on inclusion of XML based NeeS dossier as an option for the mandatory electronic dossier requirements. IWG to provide a sample of this format.

	Action Mar 11/24—The TGA to conduct industry consultation on the NeeS document with the support of Medicines Australia and GMIA, with a view to confirming industry readiness for a mandatory compliance date of 1 July 2011. *Action Mar 11/25*—The TGA to revise NeeS document to include clearer articulation of this requirement as a step towards fully electronic dossiers; outcome of XML acceptance will be included in the outcomes of the consultation process. ***Notification letter*** *Action Mar 11/26*—The TGA to amend template for notification letter to include any further detail for reasons for a variation to milestone target dates.
3.3	**Milestone 3—Consolidated s. 31 request** The IWG noted the issues identified in the report on the trial consolidated s. 31 request and that the TGA is on schedule to deliver this milestone on 30 May 2011 for the first batch of submissions. *Action Mar 11/27*—TGA to include standard text in planning letter to remind sponsors to ensure all parties (such as DMF holders) are prepared to respond to a s.31 request within the sponsor-designated timeframe.
3.4	**Milestones 4–8** ***Targets dates*** The IWG discussed the need for clarification of business rules for milestones 4-8 and in particular sponsor expectations when a milestone activity is not required, for example where no advisory committee is required or no s. 31 request is issued. The TGA advised it cannot commit to an automatic 'rolling up' of the milestone dates and advised the IWG of the following arrangements for delivery of predictable timeframes for sponsors. *Action Mar 11/28*—During the transition period as the TGA monitors implementation of the streamlined submission process, at each milestone, the TGA will deliver to sponsors a formal letter that: · reports on past planned milestone target dates and their actual delivery date · advises on future planned milestone target dates, together with an explanation for any changes. The TGA is committed to timely completion of evaluations. The TGA will capture qualitative and quantitative data that illustrates the planned versus actual performance. ***Advisory Committee (optional milestone 6)*** The IWG discussed the status of ACPM meetings for 2011 and in particular the timing for implementation of the proposed monthly meetings. The TGA advised: · following the analysis of workloads, the ACPM has ratified one of the three extraordinary meetings for 2011, in September · this analysis does highlight that a decision is based on an assessment of the need/cost/quality/benefit of monthly meetings, in recognition of the forecast low numbers per monthly meeting (6-8) and high cost of meetings. *Action Mar 11/29*—TGA to provide the IWG with detailed information to inform the decision at the next meeting about the relative cost/benefit of more frequent meetings of the ACPM to support registration decisions, particularly the ability to secure the necessary expertise on a more regular basis.
3.5	**Mandatory requirements** The IWG agreed to the proposed revisions to transitional *Mandatory requirements for an effective submission* including: *Action Mar 11/30*—TGA to deliver a document to IWG including the following revisions for 1 June 2011commencement: · specification of RMP requirements · clarity in the module 3 section to reflect recent deficiencies relating to guidelines for bioequivalence and break line data

	· clarity about the TGA's justification requirements · clarity about the TGA's process for advising sponsor of deficiencies, prior to consideration of not effective submission status.
3.6	**Communications and education activities** ***Performance and transparency*** The IWG congratulated the TGA on the newsletter and its value in sponsor engagement and awareness of issues. No changes to current arrangements were recommended. ***Sponsor education*** The IWG noted the TGA's response to issues for the generics industry and the generic sponsor training session scheduled for Tuesday 8 March 2011. The IWG agreed upon the arrangements for the next road show training in June 2011. *Action Mar 11/31*—TGA to plan the next sponsor training as follows: · 5 sessions across the same destinations with 3-hour format as per October 2011 series, with better venue for Sydney requested · partnership with ARCS to support marketing and registration management · content to focus on skills development for milestones 4–8, and an update on outcomes and issues for milestones 1–3.
4—Other business	
4.1	**Delivery of formal letters to sponsors** The IWG agreed to explore opportunities to migrate sponsors to secure email/electronic delivery of the planning/notification/s. 31 letters (current arrangement is for faxing of these letters). However it was noted that this was only feasible when all sponsors have the same functionality. *Action Mar 11/32*—TGA to explore feasibility of eBS providing platform for secure email deliver of letters to sponsors. *Action Mar 11/33*—TGA to communicate by newsletter the arrangements for secure email to sponsors (including steps for sponsors to register).
4.2	**Transition evaluation plan** The IWG agreed that details of the post transition arrangements need to be considered and informed by an independent evaluation (together with the ongoing internal qualitative/quantitative data capture). *Action Mar 11/34*—TGA to deliver at the next meeting, details of the scope of an independent evaluation of the streamlined submission process.
5—Next meetings	
5.1	Tuesday 19 April 2011 Tuesday 21 June 2011 Tuesday 23 August 2011 Tuesday 25 October 2011

4.2 NeeS consultation

The TGA invites comment on the proposed mandatory requirements for electronic submission dossiers lodged under the streamlined submission process. Full details on the consultation process, including the draft regulatory requirements are available at www.tga.gov.au. The consultation period is now open and will close on 1 May 2011. It is the intent of the TGA to mandate the regulatory requirements from 1 July 2011.